

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

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|---|---|---|-----------------------|-------------------------------------|-----------|----------------------|--------------------------|------------|----------|--------------------------|-------------|--|--------------------------|------------|----------------------------|-------------------------------------|-----------|---|--------------------------|------------|-------------------------|--------------------------|-------------|--|--------------------------|--------------|---|
| Applicant's or agent's file reference 4-3285A/USN | FOR FURTHER ACTION | | See Form PCT/IPEA/416 | | | | | | | | | | | | | | | | | | | | | | | | |
| International application No. PCT/EP2004/000571 | International filing date (day/month/year) 23.01.2004 | Priority date (day/month/year) 24.01.2003 | | | | | | | | | | | | | | | | | | | | | | | | | |
| International Patent Classification (IPC) or national classification and IPC C07C237/42, C07C275/34, C07C271/28, C07C237/30, C07D215/08, C07D217/06, C07C255/57, C07D213/82, A61K31/167, A61K31/277, A61K31/4406, A61K31/17, A61K31/27, A61K31/166, A61K31/4709, A61K31/47 | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Applicant NOVARTIS AG | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <ol style="list-style-type: none"> 1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36. 2. This REPORT consists of a total of 6 sheets, including this cover sheet. 3. This report is also accompanied by ANNEXES, comprising: <ol style="list-style-type: none"> a. <input type="checkbox"/> sent to the applicant and to the International Bureau a total of sheets, as follows: <ul style="list-style-type: none"> <input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions). <input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box. b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions). | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <ol style="list-style-type: none"> 4. This report contains indications relating to the following items: <table style="width: 100%; border: none;"> <tr> <td style="width: 10%;"><input checked="" type="checkbox"/></td> <td style="width: 15%;">Box No. I</td> <td>Basis of the opinion</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table> | | | | <input checked="" type="checkbox"/> | Box No. I | Basis of the opinion | <input type="checkbox"/> | Box No. II | Priority | <input type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability | <input type="checkbox"/> | Box No. IV | Lack of unity of invention | <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement | <input type="checkbox"/> | Box No. VI | Certain documents cited | <input type="checkbox"/> | Box No. VII | Certain defects in the international application | <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |
| <input checked="" type="checkbox"/> | Box No. I | Basis of the opinion | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. II | Priority | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. IV | Lack of unity of invention | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. VI | Certain documents cited | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application | | | | | | | | | | | | | | | | | | | | | | | | | |
| Date of submission of the demand 24.07.2004 | | Date of completion of this report 03.01.2005 | | | | | | | | | | | | | | | | | | | | | | | | | |
| Name and mailing address of the international preliminary examining authority: <div style="display: flex; align-items: center;"> <div> European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465 </div> </div> | | Authorized Officer Grammenoudi, S Telephone No. +49 89 2399-8324 | | | | | | | | | | | | | | | | | | | | | | | | | |



**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/EP2004/000571

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-114 as originally filed

Claims, Numbers

1-39 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/EP2004/000571

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|-------------|----------------------------------|
| Novelty (N) | Yes: Claims | 4-6,9-12,14-17,20-23,25-36,38,39 |
| | No: Claims | 1-3,7,8,13,18,19,24,37 |
| Inventive step (IS) | Yes: Claims | |
| | No: Claims | 1-39 |
| Industrial applicability (IA) | Yes: Claims | 1-24,33-39 |
| | No: Claims | 25-32 |

2. Citations and explanations (Rule 70.7):

see separate sheet

**INTERNATIONAL PRELIMINARY
REPORT ON PATENTABILITY
(SEPARATE SHEET)**

International application No.

PCT/EP2004/000571

The numbering of the documents D1-D36 corresponds to the order given in the search report i.e.

D1= WO-A-01/90094

D2= WO-A-03/40108

D3= WO-A-94/01113

D4= DE-A- 817 911

D5= DE-A-2 756 771

D6= US-A-3 963 745

D7= CH-A-242 949

D8= DE-A-2 316 644

D9= DE-A-2 625 285

D10= DE-A-2 459 380

D11= US-A-3 646 048

D12= DE-A-2 242 007

D13= DE-A-2 505 447

D14-D36 = database Beilstein

D37= Römpps Chemie-Lexikon, 10. Auflage, 1996

1. The present application relates to amide derivatives acting as inhibitors of 11 β -hydroxysteroid dehydrogenase type 1 (11 β -HSD1), to pharmaceutical compositions comprising them and to their use in treating conditions associated with 11 β -HSD1 activity.
2. Documents D2-D36 disclose compounds which are prejudicial to the novelty of present claims 1-3,7,8, 13, 18, 19, 24 and 37 (see D2, page 131, Example 6 and page 132, Example 6.1; D3, Preparations 1-6 and pages 126-166; D4, Examples 1, 3-7, 11 and 13; D5, Example 19 and Example 19 in combination with the methyl esters produced in Examples 1, 4, 6, 8, 9, 11 and 15 ; D6, Example 6; D7, Example; D8, Examples 4, 6, 9, 31, 55, 62 and 65; D9, page 39, lines 1-6; D10, page 14, ultimate line, page 32, lines 12-13; D11, Example 15 and 16; D12, Examples 1 and 2, page 6, lines 15-18; D13, Example 20). Accordingly, the subject-matter of claims 1-3,7,8, 13, 18, 19, 24 and 37 does not meet the requirements of Art. 33(2) PCT.
3. The subject-matter of the remaining claims is deemed novel. In the light of D1(see page 1, lines 1-10;claim 1), the problem to be solved by the present application is to provide alternative 11 β -HSD1 inhibitors.

This technical problem can only be regarded as having been solved if, in deciding the issue under Article 33(3) PCT, it would be credible that all compounds of formula I possess said modulating activity.

It is accepted as common general knowledge that the properties of chemical compounds largely depend on their chemical structure and that even small structural differences may cause major differences in biological activity. The term "optionally substituted" as used in claims 1-24 means that the groups in question may be substituted by absolutely anything. It is thus inherently quite unlikely that each of the claimed compound is capable of solving the above technical problem. Moreover, there is no instruction in the description which would enable the skilled person to prepare such derivatives.

Accordingly, the subject-matter of claim 1-39 does not satisfy the requirements of Articles 33(3) and 5 PCT.

4. For the assessment of the present claims 25-32 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment
5. The clarity of claims and their consistency with the description is of the utmost importance for the purposes of formulating an opinion on the questions whether the claimed invention appears to be novel and to involve an inventive step in view of their function in defining the matter for which protection is sought. As set out in PCT Guidelines III-4.2., the terms used in a claim are to be interpreted as having the meaning and scope which they normally have in the relevant art. Furthermore, the meaning of such terms must be clear from the wording of the claim alone.
- 5.1. The definition of the terms "alkyl", "alkenyl", "alkylene", "cycloalkyl", "carbamoyl", "aryl" and "heterocyclyl" on pages 3-7 is not in consistency with the commonly accepted meaning of these terms (cf. D37, pages 116, 109, 111, 843, 598, 268, 1739). For instance, the aforementioned expressions do not normally involve any upper limit restricting the number of the participating carbon atoms or ring atoms.

Nor there exists any restriction concerning the position of the double and triple bond(s) in "alkenyl" or "alkynyl" respectively. Likewise, the terms "aryl", and "heterocyclyl" do not embrace substituted aryl and heterocyclyl moieties and the heteroatoms in heterocycles includes not merely nitrogen, oxygen, and sulphur. This inconsistency between claims 1-24 and the description renders the scope of the claims unclear (Art. 6 PCT).

- 5.2. The terms "lower alkyl" and "lower alkoxy" used in claims 1-4 and 7-23 are ambiguous because they do not have a generally accepted meaning with respect to the maximum number of carbon atoms constituting the groups. As a result, claims 1-4 and 7-23 lack clarity contrary to the requirements of Article 6 PCT.
- 5.3. The term "about" used in connection with ranges (cf. pages 31, 33 and 35) as well as the phrases "and the like" (cf. pages 3-8 and 25) and "etc." (cf. page 28) render the scope of the application unclear (Art. 6 PCT).
6. The statements "which are herein incorporated by reference" (cf. page 32, penultimate line) and "The corresponding content thereof is hereby incorporated by reference" (cf. page 33, second paragraph) contradict the requirements of Rules 5.1(a)(iii) and 9.1(iv) PCT.
7. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in document D1 is not mentioned in the description, nor is this document identified therein.